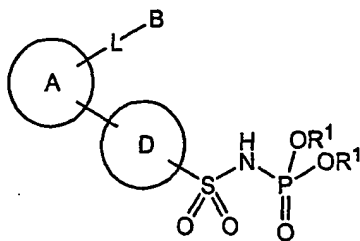


## CLAIMS

1.- A compound of general formula I:



I

wherein:

each  $R^1$  independently represents hydrogen,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl, phenyl, heteroaryl or phenyl/ $C_{1-3}$  alkyl, where all phenyl and heteroaryl rings can be optionally substituted with one or more halogen,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkoxy groups, or both substituents  $R^1$  may be taken together to form a saturated or partially unsaturated 5- or 6-membered ring, which can be optionally fused to a benzene ring;

A represents an unsaturated or partially unsaturated 5- or 6-membered ring which can optionally contain from 1 to 3 heteroatoms selected from N, O and S, where the substituents L and D are placed on adjacent atoms of ring A, and where additionally A can be optionally substituted with one or more substituents  $R^2$ ;

L represents a single bond, -O-, -S- or -NR<sup>3</sup>-;

B represents  $C_{1-6}$  alkyl or a ring selected from phenyl, heteroaryl and  $C_{3-7}$  cycloalkyl, where all said rings can be optionally substituted with one or more substituents  $R^4$ ;

D represents phenyl or pyridine, which can be both optionally substituted with one or more halogens;

the groups A and -SO<sub>2</sub>NHP(O)(OR<sup>1</sup>)<sub>2</sub> are placed on ring D in *para* position with respect to one another;

each  $R^2$  independently represents halogen, cyano, nitro, carboxy,  $C_{1-4}$  alkyl,  $C_{2-4}$  alkenyl,  $C_{2-4}$  alkynyl,  $C_{1-4}$  haloalkyl, hydroxy,  $C_{1-4}$  hydroxyalkyl,  $C_{1-4}$  alkoxy,  $C_{1-4}$  haloalkoxy,  $C_{1-4}$  alkylthio, amino,  $C_{1-4}$  alkylamino,  $C_{1-4}$  dialkylamino, formyl,  $C_{1-4}$  alkylcarbonyl,  $C_{1-4}$  alkoxycarbonyl,  $C_{1-4}$  haloalkoxycarbonyl,  $C_{1-4}$  alkoxy/ $C_{1-3}$  alkyl,

C<sub>1-4</sub> alkylcarbonyloxyC<sub>1-3</sub> alkyl, C<sub>3-7</sub> cycloalkylC<sub>1-4</sub> alkoxyC<sub>1-3</sub> alkyl or C<sub>3-7</sub> cycloalkoxyC<sub>1-3</sub> alkyl, or two substituents R<sup>2</sup> on the same carbon atom can be taken together to form an oxo group;

R<sup>3</sup> represents hydrogen or C<sub>1-4</sub> alkyl;

- 5 each R<sup>4</sup> independently represents halogen, cyano, nitro, carboxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, hydroxy, C<sub>1-4</sub> hydroxyalkyl, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> haloalkoxy, C<sub>1-4</sub> alkylthio, amino, C<sub>1-4</sub> alkylamino, C<sub>1-4</sub> dialkylamino, formyl, C<sub>1-4</sub> alkylcarbonyl, C<sub>1-4</sub> alkoxy carbonyl or C<sub>1-4</sub> haloalkoxy carbonyl, or two substituents R<sup>4</sup> on the same carbon atom can be taken together to form an oxo group, and additionally one of
- 10 the substituents R<sup>4</sup> can represent a saturated, unsaturated or partially unsaturated 5- or 6-membered ring which can optionally contain from 1 to 3 heteroatoms selected from N, O and S and which can be optionally substituted with one or more substituents R<sup>5</sup>;

- each R<sup>5</sup> independently represents halogen, hydroxy, nitro, cyano, amino, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-4</sub> alkoxy or C<sub>1-4</sub> alkylcarbonyl, or two substituents R<sup>5</sup> on the same carbon atom can be taken together to form an oxo group; and
- 15 heteroaryl in the above definitions represents pyridine, pyrazine, pyrimidine or pyridazine;
- and the salts and solvates thereof.

- 20 2.- A compound according to claim 1 wherein A represents imidazole, pyrazole, isoxazole, oxazole, thiazole, 2,5-dihydrofuran, thiophene, pyridine, 4H-pyran, cyclopentene, 2,3-dihydrooxazole or 4,5-dihydropyrazole which can be optionally substituted with one to four substituents R<sup>2</sup>.

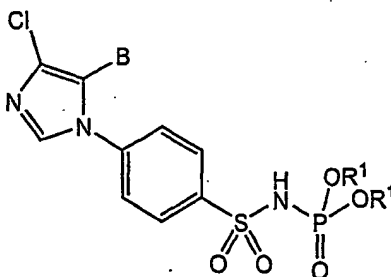
- 3.- A compound according to claim 2 wherein A represents imidazole, pyrazole, isoxazole, oxazole, 2,5-dihydrofuran or 4H-pyran which can be optionally substituted with one to four substituents R<sup>2</sup>.
- 25

4.- A compound according to claim 3 wherein A represents imidazole, pyrazole, isoxazole or oxazole which can be optionally substituted with one or two substituents R<sup>2</sup>.

- 30 5.- A compound according to claim 4 wherein A represents imidazole which can be optionally substituted with one substituent R<sup>2</sup>.

6.- A compound according to any of claims 1 to 5 wherein each R<sup>2</sup> independently represents halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> haloalkyl, or two substituents R<sup>2</sup> on the same carbon atom can be taken together to form an oxo group.

- 7.- A compound according to any of claims 1 to 6 wherein D represents either phenyl optionally substituted with a fluoro atom or D is pyridine.
- 8.- A compound according to claim 7 wherein D represents phenyl optionally substituted with a fluoro atom.
- 5 9.- A compound according to claim 8 wherein D represents phenyl.
- 10.- A compound according to any of claims 1 to 9 wherein L represents a single bond or -O-.
- 11.- A compound according to claim 10 wherein L represents a single bond.
- 12.- A compound according to any of claims 1 to 11 wherein B represents phenyl, heteroaryl or C<sub>3-7</sub> cycloalkyl, which can all be optionally substituted with one to three substituents R<sup>4</sup>.
- 13.- A compound according to claim 12 wherein B represents phenyl optionally substituted with one to three groups R<sup>4</sup> or B represents cyclohexyl.
- 14.- A compound according to claim 13 wherein B represents phenyl optionally substituted with one to three groups R<sup>4</sup>.
- 15 15.- A compound according to claim 10 wherein L represents -O-.
- 16.- A compound according to claim 15 wherein B represents C<sub>1-6</sub> alkyl or phenyl optionally substituted with one to three substituents R<sup>4</sup>.
- 17.- A compound according to claim 16 wherein B represents isopropyl or phenyl optionally substituted with one to three substituents R<sup>4</sup>.
- 20 18.- A compound according to any of claims 1 to 17 wherein each R<sup>4</sup> independently represents halogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy or C<sub>1-4</sub> haloalkyl.
- 19.- A compound according to claim 1 of formula Id:



Id

wherein:

B represents phenyl optionally substituted with one to three groups R<sup>4</sup>; and each R<sup>4</sup> independently represents halogen, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy or C<sub>1-4</sub>

haloalkyl.

20.- A compound according to claim 19 wherein B represents 3-fluoro-4-methoxyphenyl.

21.- A compound according to any of claims 1 to 20 wherein each R<sup>1</sup>  
5 independently represents hydrogen, C<sub>1-6</sub> alkyl or phenyl optionally substituted with one or more halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy groups.

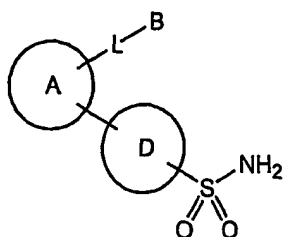
22.- A compound according to claim 1 selected from:

- diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- 10 N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;
- trisodium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- tripotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- 15 dipotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- calcium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- 20 tricalcium di-[N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate];
- diethyl N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic  
25 acid;
- diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- 30 diethyl N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidate;
- N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidic acid;
- diethyl N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidate;

- N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidic acid;  
 diethyl N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidate; and  
 N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidic  
 5 acid;  
 and the salts and solvates thereof.
- 23.- A compound according to claim 1 selected from:
- diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 10 diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;  
 diethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;  
 ethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;  
 15 ethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;  
 N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;  
 20 trisodium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 tripotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 dipotassium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 25 calcium N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 tricalcium di-[N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate];  
 30 diethyl N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;  
 N-[4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid;

- diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- diphenyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;
- 5 dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate;
- dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;
- dimethyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate potassium salt;
- 10 methyl N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidate sodium salt;
- diethyl N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidate;
- 15 N-[4-[5-(*p*-tolyl)-3-(trifluoromethyl)pyrazol-1-yl]phenylsulfonyl]phosphoramidic acid;
- diethyl N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidate;
- N-[4-(5-methyl-3-phenylisoxazol-4-yl)phenylsulfonyl]phosphoramidic acid;
- diethyl N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidate; and
- 20 N-[4-[4-cyclohexyl-2-methyloxazol-5-yl]-2-fluorophenylsulfonyl]phosphoramidic acid.
- 24.- A compound according to claim 1 wherein the compound is N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid, and
- 25 the salts and solvates thereof.
- 25.- Process for preparing a compound of formula I according to claim 1 which comprises:
- (a) when in a compound of formula I each R<sup>1</sup> is different from hydrogen, reacting a sulfonamide of formula II

46



II

wherein A, L, B and D have the meaning described in claim 1, with a compound of formula III

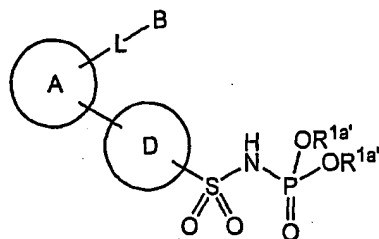


III

5

wherein X represents H or Cl and wherein each  $\text{R}^{1a}$  independently represents any of the meanings described for  $\text{R}^1$  in claim 1 except for hydrogen, in the presence of a base, or alternatively, reacting a sulfonamide of formula II in which the group  $-\text{SO}_2\text{NH}_2$  is in anionic form with a compound of formula III;

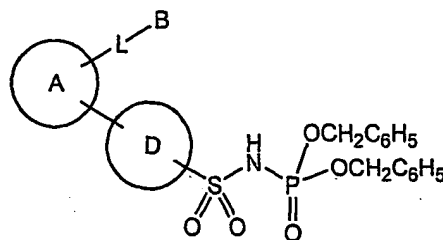
- 10 (b) when in a compound of formula I each  $\text{R}^1$  represents hydrogen, hydrolysing a compound of formula Ia'



Ia'

wherein A, L, B and D have the meaning described in claim 1 and wherein  $\text{R}^{1a'}$  represents any of the meanings described for  $\text{R}^1$  in claim 1 except for hydrogen

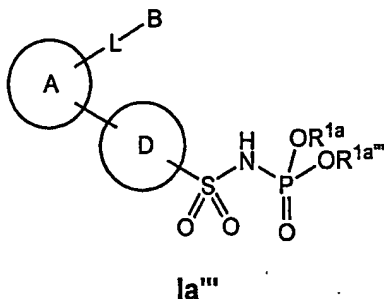
- 15 and benzyl, or alternatively, hydrogenating a compound of formula Ia''



Ia''

wherein A, L, B and D have the meaning described in claim 1;

(c) when in a compound of formula I one of the substituents  $R^1$  represents hydrogen and the other is different from hydrogen, monodealkylating a compound of formula Ia'''



5 wherein A, L, B, D and  $R^{1a}$  have the meaning described above and wherein  $R^{1a''}$  represents  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl or phenyl $C_{1-3}$  alkyl, where the phenyl group can be optionally substituted with one or more halogen,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkoxy groups;

(d) transforming, in one or a plurality of steps, a compound of formula I into  
10 another compound of formula I; and

(e) if desired, after the above steps, reacting a compound of formula I with a base or an acid to give the corresponding addition salt.

26.- A pharmaceutical composition which comprises an effective amount of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically  
15 acceptable salt or solvate thereof and one or more pharmaceutically acceptable excipients.

27.- Use of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment or prevention of diseases mediated by  
20 cyclooxygenase.

28.- Use of a compound of formula I according to any of claims 1 to 24 or a pharmaceutically acceptable salt or solvate thereof for the manufacture of a medicament for the treatment or prevention of diseases mediated by cyclooxygenase-2.

29.- Use according to claim 28 wherein the disease mediated by cyclooxygenase-2 is selected from inflammation, pain, fever, pathologies associated with prostanoid-induced smooth muscle contraction, preneoplastic disorders, cancer, cerebral infarction, epilepsy, type I diabetes, neurodegenerative diseases and



vascular diseases with an inflammatory component.

30.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is selected from inflammation, pain and fever.

31.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a preneoplastic disorder.

32.- Use according to claim 31 wherein the preneoplastic disorder is familial adenomatous polyposis.

33.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is cancer.

34.- Use according to claim 33 wherein the cancer is a gastrointestinal cancer.

35.- Use according to claim 34 wherein the gastrointestinal cancer is colon cancer.

36.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a neurodegenerative disease.

37.- Use according to claim 36 wherein the neurodegenerative disease is selected from dementia, Parkinson's disease and amyotrophic lateral sclerosis.

38.- Use according to claim 37 wherein the dementia is Alzheimer's disease.

39.- Use according to claim 29 wherein the disease mediated by cyclooxygenase-2 is a vascular disease with an inflammatory component.

40.- Use according to claim 39 wherein the vascular disease with an inflammatory component is atherosclerosis.

41.- Use according to claim 28 wherein the disease mediated by cyclooxygenase-2 is selected from the group consisting of: pain resulting from surgery or dental surgery; low back and neck pain; headache; toothache; pain associated with cancer; neuralgia; arthritis, including rheumatoid arthritis and juvenile arthritis; degenerative joint diseases, including osteoarthritis; gout; ankylosing spondylitis; tendinitis; pain and/or inflammation associated with traumatism such as sprains, strains and other similar injuries, such as those produced during sport performance; synovitis; myositis; dysmenorrhea; inflammatory bowel disease; ocular inflammatory diseases, including conjunctivitis and endophthalmitis; corneal transplants; skin inflammatory diseases, including psoriasis, burns, eczema and dermatitis; systemic inflammatory processes, including sepsis and pancreatitis; bursitis; lupus erythematosus; common cold; rheumatic fever; symptoms associated with influenza or other viral infections; preterm labour;

asthma; bronchitis; familial adenomatous polyposis; cancer, including liver, bladder, pancreas, ovary, prostate, cervix, lung, breast, skin cancer and gastrointestinal cancers such as colon cancer; cerebral infarction; epilepsy; type I diabetes; dementia, including Alzheimer's disease; Parkinson's disease; amyotrophic lateral sclerosis; and atherosclerosis.

5